

The Rejection of Claims 13 and 15-22 under 35 U.S.C. §112, second paragraph

Claims 13 and 15-22 stand rejected as indefinite. Applicant respectfully traverses.

The term "GPNMB" is objected to as having multiple meanings and being a mere laboratory term. However, GPNMB is actually a term of art. This is the designation which those of skill in the art have given to a particular gene. The specification at page 26, Table 2, last line, describes the gene with a gene name (Glycoprotein (transmembrane) *nmb*), a gene symbol (*GPNMB*), a cellular location (membrane), a GenBank number (X76534), primer pairs for amplification of the gene (SEQ ID NO: 15 and 16), and a literature citation (Weterman, 1995, *Int. J. Cancer* 60: 73-81).

If one uses the GenBank number one finds a particular amino acid sequence for the protein:

MECLYYFLGFLLLAARLPDAAKRFHDLGNERP SAYMREHNQLNGWSSDENDWNEK
LYPVWKRGD MRWKNWSWKGRRVQAVLTSDSPALVGSNITFAVNLIFFRCQKEDANGNI
VYEKNCRNEAGLSADPYVYNWTAWSESDSGENG TGQSHHNVPFDGKPPFHPGWRR
WNFIYVFHTL GQFYQKLGRCSVRVSVNTANVT LGPQLMEVTVYRRHGRSTINYKWSFG
DNTGLFVSTNHTVNHTYVLNGTFSLNLT VKAAAPGPCPPPPPPRPSKPTPSLGPAGDNP
LELSRIPDENCQINRYGHFQATITIV EGILEVNIQM TDVLMVPVWPESLIDFVVT CQGSIP
TEVCTIISDPTCEITQNTVCS PVDVDEMCLLTVRRTFNGSGTYCVNLT LGDDTSLALTSTL
ISVPDRDPASPLRMANSALISVGCLAIFVTVISLLVYKKHKEYNPIENSPGNVVR SKGLSV
FLNRAKAVFFPGNQEKDPLLKNQEFKGVS. See Tab A.

Thus the term GPNMB is neither indefinite nor a laboratory term. It has a specific meaning in the art which one of ordinary skill in the art would know, given the teachings of the specification. Although applicants do not believe it to be necessary, claim 13 has been amended to recite the longer name "Glycoprotein (transmembrane) *nmb*."

The term "contacting" in the phrase "contacting cells with an antibody" of claim 13 is said to be unclear. The Patent Office asks whether applicant intends "for the compounds to be delivered by placing the antibody in a cell of a glioblastoma."¹ The step of contacting does not require that an antibody be placed *in* a cell. It requires that the antibody be placed in contact

¹ If the question arose due to the missing preposition in the claim as filed, that missing preposition ("with") has now been inserted by amendment.

with a cell. If the cell is in culture, then the antibody is placed in the culture medium. If the cell is in an animal, then the antibody is delivered into the animal so that the antibody can *contact* the cell.

The plain meaning of the word "contacting" is intended and there is no indefiniteness. The dictionary² defines the verb "to contact" as "to bring or put into contact." The noun "contact" is defined as "the coming together or touching of two objects or surfaces." These meanings are what applicant intends, as discussed with particularity above with regard to cells and antibodies.

The term "extracellular epitope" is also said to be indefinite because the metes and bounds cannot be defined. The Office Action explains that any combination of three or more amino acids found within the extracellular domain of GPNMB can be considered an epitope. Even if the definition of an extracellular epitope is accurately provided by the Office Action, it does not follow that the term is indefinite. The extracellular domain of GPNMB is a known domain of a known protein. The claim simply requires that the antibody which is used be capable of binding to the extracellular domain. The claim is clear and definite as written.

The Rejection of Claims 13 and 15-22 Under 35 U.S.C. §112, first paragraph

Claims 13 and 15-22 are rejected as not enabled by the specification. The specification allegedly does not enable any person skilled in the art to practice the invention commensurate in scope with these claims. This rejection is respectfully traversed.

The Office Action provides its rationales for the rejection at pages 4 and 5. They are quoted below and addressed individually.

- *"Nowhere in the specification does it specifically teach the delivery of an agent to a specific epitope of GPNMB, because the GPNMB protein has never actually been defined in the specification. There is little information of the protein itself."*

The Office Action urges that the protein is not defined. However, as pointed out above, the GPNMB protein was known in the art, and the specification references its complete amino

² The American Heritage Dictionary, second college edition, Houghton Mifflin Company, Boston, 1982.

acid sequence in GenBank. It is not clear what additional information about the protein might be necessary to practice the invention.

Applicants have applied the SMART (Simple Modular Architecture Research Tool) tool to automatically identify the extracellular domain of GPNMB. SMART is made available to the public by the European Molecular Biology Laboratory on the Internet. As shown at Tab B, amino acids 1 to 483 have a >0.98 probability of being extracellular. Thus one of ordinary skill in the art would have no trouble identifying the extracellular domain or making antibodies which specifically bind to it.

- *"The specification does not teach whether the protein even actually exists."*

The specification implicitly teaches that the protein exists. The specification teaches throughout the use of antibodies specific for the protein. The specification teaches throughout the detection of elevated expression levels using Western blotting, enzyme-linked immunosorbent assay, radioimmunoassay, and fluorescence activated cell sorting. If the protein did not exist, then these teachings would be for naught.

Applicants may not, *arguendo*, have proven that the protein exists. However, applicants are not obliged to prove such things. The Patent Office is obliged to assume the truth of the specification's teachings unless it has good reason to doubt it. *See*, MPEP §2107.02, which quotes from *In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) as follows:

[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support (emphasis added).

Thus, the specification's alleged failure to explicitly teach that the protein exists cannot render the specification not enabling.

- *"It is a well established fact that in normal circumstances, the level of transcription parallels that of translation, however, in certain circumstances, the level of mRNA transcription is uncoupled from protein translation. Therefore, given the fact that it is possible for some transcription and translation events to be unparallelled, it is possible GPNMB may not be translated from the unregulated mRNA detected in the instant invention."*(citations committed)

The Office Action speculates that GPNMB protein translation may be uncoupled from GPNMB mRNA transcription. This speculation is contrary to what the Office Action itself sets out as the "established fact in normal circumstances." There is no factual or evidentiary basis provided by the Office Action for asserting that GPNMB departs from the normal circumstance. However, as stated in the MPEP, there must be a "reason to doubt the objective truth of the statements contained therein." Mere speculation about a possibility is not a reason to doubt. Thus this rationale cannot properly serve as a basis for rejecting the claims as not enabled.

- *"How would one of skill in the art know whether there are even enough epitopes present on the surface of a glioblastoma for the method to be effective in delivering an agent."*

The Office Action speculates that one requires a certain number of epitopes to make delivery effective. However, the specification teaches that the GPNMB protein is highly expressed in glioblastoma. See, e.g., Figure 3. Moreover, the amino acid sequence of GPNMB protein indicates that 483/560 residues are likely to be extracellular (i.e., 86 % of the protein). See Tab B. Thus, the record evidence suggests that there will be sufficient extracellular epitopes on the surface of glioblastoma cells. The imputation to the contrary has no factual or scientific basis.

- *"If there is only a small percentage of protein found on the surface of the glioblastoma cell, then the antibody conjugate that is administered is left circulating in the blood stream thereby eliciting anti-idiotypic antibodies."*

The Office Action speculates that administration of an antibody-conjugate may cause a presumably undesirable side effect, elicitation of anti-idiotypic antibodies. The Office Action does not explain how that would render the claimed method unworkable. Nonetheless, this is again mere speculation, without the slightest bit of evidentiary support or scientific basis.

- *"Because the working examples of the instant invention have only provided a method of screening, amplification, hybridization, and other general methods of probing, it is not commensurate in scope to the claims that read on methods of delivering a reagent using an antibody to GPNMB."*

The Office Action makes the false equation that the scope of the *working examples* must be commensurate with the scope of the claims. In fact, the law requires that the scope of the *specification's teachings as a whole* must be commensurate with the scope of the claims ("the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims." MPEP §2164.08. The absence of working examples is not determinative of non-enablement. "How a teaching is set forth, by specific example or broad terminology, is not important." MPEP §2164.08.

The Patent Office has not met its burden in showing that the specification does not provide enablement that is commensurate with the scope of the claims. The burden is on the Patent Office to "back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement [of the application]." See MPEP § 2164.04. The Patent Office has simply used speculation without ever providing evidence inconsistent with the teachings of the specification. Withdrawal of this rejection is requested because the Patent Office has not made a *prima facie* case of non-enablement.

The Rejection of Claims 13, 15, 18-20 and 22 under 35 U.S.C. §102(b)

Claims 13, 15, 18-20, and 22 stand rejected as anticipated by Johnson (U.S. 5,352,447). This rejection is respectfully traversed.

Johnson is cited as teaching use of an antibody that specifically recognizes the transferrin receptor.

Claims 13, 15, 18-20 and 22 are directed to use of an antibody that specifically binds to an extracellular epitope of GPNMB.

GPNMB and transferrin receptor are two distinct proteins. The office action provides no evidence whatsoever that they are the same protein or even that they are similar proteins. In the absence of any such evidence, there is no reasonable basis on which to conclude that these proteins share epitopes. There is no reasonable basis to conclude that antibodies specific for transferrin receptor would specifically bind to GPNMB. The PTO has failed to meet its burden in presenting a *prima facie* case of anticipation, inherency, or equivalence.

Current estimates of the complexity of the human genome are in the range of 40,000 genes. The assumption of a one-to-one correspondence of genes-to-proteins would lead to an estimate of 40,000 proteins in the human proteome. There is no reason to believe that any two of 40,000 proteins selected at random would be similar in sequence.

The PTO justifies its conclusion of equivalence of the transferrin receptor and GPNMB on the basis of the failure of applicants to provide the sequence of GPNMB. However, as discussed above, the sequence of GPNMB is known in the art and is cited in the specification. No sequence for transferrin receptor is found in the cited Johnson patent. Nonetheless, applicants have compared the sequences of human transferrin receptor proteins 1 (Tab C) and 2 (Tab D) to the sequence of GPNMB (Tab A). The NCBI's Blast 2 Sequences tool was used. No significant similarity was found. See Tabs E and F.

The Rejection of Claims 13, 15, and 18-21 under 35 U.S.C. §103(a)

Claims 13, 15, and 18-21 stand rejected as unpatentable over Lazarus in view of either Reiter or Maynard. This rejection is respectfully traversed.

Lazarus, the primary reference, is cited as teaching the assessment of anti-NMB antibodies. The PTO asserts that NMB of Lazarus is also known as GPNMB. This, however, is a false assertion. Lazarus teaches that Neuromedin B is a decapeptide, *i.e.*, a ten-amino acid residue peptide. See page 161, column 1, first sentence. The sequence of neuromedin B is provided in Lazarus' Table 1, line 1: GNLWATGHFM-NH₂. This sequence does not appear in

the sequence of GPNMB (NP_002501). Thus the basis for the rejection must collapse as NMB and GPNMB are not the same protein, as erroneously asserted by the PTO.

Lazarus' neuromedin B decapeptide is produced *in vivo* from a 121 amino acid-residue protein. See NP_066563, particularly residues 47-56 (Tab G).

Applicants compared the NMB, NP_066563, 121 residue sequence to the 560 residue GPNMB sequence of NP_002501 (Tab H) using the Blast 2 Sequences program of the NCBI.³ No significant similarity was found. (See Tab I.) Thus, the PTO's contention that NMB and GPNMB are the same is simply not true.

Applicants also searched the entire GenBank CDS translations using BlastP and the neuromedin B, 121-residue sequence. Of the 18 hits, none were GPNMB. See Tab J.

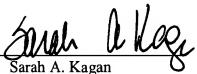
Reiter and Maynard do not remedy this deficiency. Both are cited as teaching "conjugation of antibodies in general to either toxic agents or labels for the treatment or imaging of cancer." Thus, even if one were motivated to combine the teachings of the cited reference, one would not achieve the present invention. None of the cited references teaches antibodies to GPNMB.

Withdrawal of this rejection is respectfully requested.

Respectfully submitted,

BANNER & WITCOFF, LTD.

Dated: July 14, 2003

By: 
Sarah A. Kagan
Registration No. 32,141

Customer No. 22907

³ Note that the protein sequences are derived from the gene sequence M21551.1 and X76534.1. Each of these gene sequences is cited in the specification at Table 2.



Nucleotide

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Bio

Search for
 Limits Preview/Index History Clipboard Details
 Display Show: Send to Get Subsequence

1: X76534. H.sapiens NMB mRNA...[gi:666042]

Links

LOCUS HSNMB 2669 bp mRNA linear PRI 09-FEB-1995
 DEFINITION H.sapiens NMB mRNA.
 ACCESSION X76534
 VERSION X76534.1 GI:666042
 KEYWORDS NMB gene.
 SOURCE Homo sapiens (human)
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (bases 1 to 2669)
 AUTHORS Weterman, M.A., Ajubi, N., van Dinter, I.M., Degen, W.G., van
 Muijen, G.N., Ruitter, D.J. and Bloemers, H.P.
 TITLE nmb, a novel gene, is expressed in low-metastatic human melanoma
 cell lines and xenografts
 JOURNAL Int. J. Cancer 60 (1), 73-81 (1995)
 MEDLINE 95113576
 PUBMED 7814155
 REFERENCE 2
 AUTHORS Weterman, M.
 TITLE Direct Submission
 JOURNAL Submitted (03-DEC-1993) M. Weterman, University of Nijmegen, Dept
 of Biochemistry, PO Box 9101, 6500 HB Nijmegen, NETHERLANDS
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BASE COUNT 752 a 595 c 597 g 725 t
 ORIGIN

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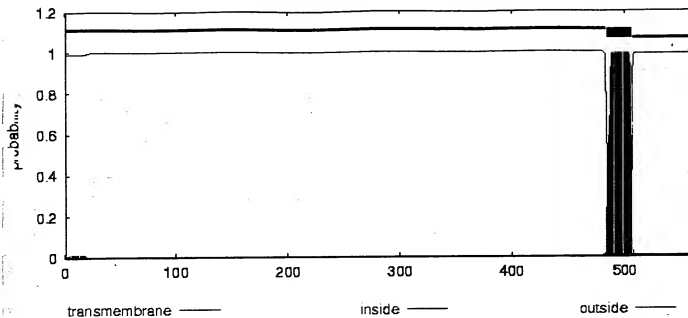
//

Disclaimer | Write to the Help Desk
 NCBI | NLM | NIH

Mar 17 2003 10:55:57

Tab B

TMHMM posterior probabilities for Sequence



BEST AVAILABLE COPY

Tab B

Sarah Kagan

From: Ben Aghdasi
Sent: Friday, April 25, 2003 2:48 PM
To: Sarah Kagan
Subject: I have also left a copy of the following results on you desk.



TMHMM
result.gif

Sarah,

This program predicts extracellular and intercellular of the protein.

The figure is in color and listed below is probability table used to draw the figure above.

As seen from 1-483 amino acid has a probability of >0.98 to be Extracellular
and from 509-560 amino acid has a probability of >0.98 to be intercellular

Probability table.

Sequence

#	AA	inside	membr	outside
1	M	0.01149	0.00000	0.98851
2	E	0.00781	0.00368	0.98851
3	C	0.00452	0.00697	0.98851
4	L	0.00452	0.00708	0.9884
5	Y	0.00107	0.01057	0.98837
6	Y	0.00107	0.01057	0.98837
7	F	0.00092	0.01071	0.98837
8	L	0.00092	0.01071	0.98837
9	G	0.00092	0.01071	0.98837
10	F	0.00092	0.01071	0.98837
11	L	0.00092	0.01071	0.98837
12	L	0.00092	0.01071	0.98837
13	L	0.00092	0.01071	0.98837
14	A	0.00092	0.01071	0.98837
15	A	0.00092	0.01071	0.98837
16	R	0.00092	0.01071	0.98837
17	L	0.00092	0.01068	0.98841
18	P	0.00092	0.01040	0.98868
19	L	0.00093	0.01019	0.98888
20	D	0.00102	0.00527	0.99371
21	A	0.00103	0.00344	0.99553
22	A	0.00104	0.00299	0.99596
23	K	0.00105	0.00017	0.99878
24	R	0.00105	0.00011	0.99884
25	F	0.00105	0.00007	0.99888
26	H	0.00106	0.00005	0.9989
27	D	0.00106	0.00003	0.99892
28	V	0.00106	0.00002	0.99892
29	L	0.00106	0.00002	0.99893
30	G	0.00106	0.00000	0.99895
31	N	0.00106	0.00000	0.99895
32	E	0.00106	0.00000	0.99895
33	R	0.00106	0.00000	0.99895
34	P	0.00106	0.00000	0.99895
35	S	0.00106	0.00000	0.99895
36	A	0.00106	0.00000	0.99895
37	Y	0.00106	0.00000	0.99895
38	M	0.00106	0.00000	0.99895
39	R	0.00106	0.00000	0.99895
40	E	0.00106	0.00000	0.99895
41	H	0.00106	0.00000	0.99895
42	N	0.00106	0.00000	0.99895

43 Q	0.00106	0.00000	0.99895
44 L	0.00106	0.00000	0.99895
45 N	0.00106	0.00000	0.99895
46 G	0.00106	0.00000	0.99895
47 W	0.00106	0.00000	0.99895
48 S	0.00106	0.00000	0.99895
49 S	0.00106	0.00000	0.99895
50 D	0.00106	0.00000	0.99895
51 E	0.00106	0.00000	0.99895
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53 D	0.00106	0.00000	0.99895
54 W	0.00106	0.00000	0.99895
55 N	0.00106	0.00000	0.99895
56 E	0.00106	0.00000	0.99895
57 K	0.00106	0.00000	0.99895
58 L	0.00106	0.00000	0.99895
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60 P	0.00106	0.00000	0.99895
61 V	0.00106	0.00000	0.99895
62 W	0.00106	0.00000	0.99895
63 K	0.00106	0.00000	0.99895
64 R	0.00106	0.00000	0.99895
65 G	0.00106	0.00000	0.99895
66 D	0.00106	0.00000	0.99895
67 M	0.00106	0.00000	0.99895
68 R	0.00106	0.00000	0.99895
69 W	0.00106	0.00000	0.99895
70 K	0.00106	0.00000	0.99895
71 N	0.00106	0.00000	0.99895
72 S	0.00106	0.00000	0.99895
73 W	0.00106	0.00000	0.99895
74 K	0.00105	0.00000	0.99895
75 G	0.00104	0.00002	0.99894
76 G	0.00103	0.00003	0.99894
77 R	0.00102	0.00004	0.99893
78 V	0.00099	0.00008	0.99893
79 Q	0.00099	0.00010	0.99892
80 A	0.00090	0.00026	0.99884
81 V	0.00088	0.00032	0.9988
82 L	0.00088	0.00032	0.99879
83 T	0.00088	0.00033	0.99879
84 S	0.00088	0.00034	0.99879
85 D	0.00088	0.00034	0.99878
86 S	0.00088	0.00036	0.99877
87 P	0.00087	0.00036	0.99876
88 A	0.00087	0.00037	0.99876
89 L	0.00087	0.00037	0.99876
90 V	0.00087	0.00037	0.99876
91 G	0.00087	0.00037	0.99876
92 S	0.00087	0.00037	0.99876
93 N	0.00087	0.00037	0.99876
94 I	0.00087	0.00037	0.99876
95 T	0.00087	0.00037	0.99876
96 F	0.00087	0.00036	0.99876
97 A	0.00087	0.00036	0.99877
98 V	0.00088	0.00034	0.99878
99 N	0.00088	0.00031	0.99881
100 L	0.00088	0.00031	0.99881
101 I	0.00089	0.00028	0.99883
102 F	0.00091	0.00025	0.99884
103 P	0.00100	0.00008	0.99892
104 R	0.00105	0.00001	0.99894
105 C	0.00105	0.00001	0.99894
106 Q	0.00105	0.00000	0.99894
107 K	0.00106	0.00000	0.99894
108 E	0.00106	0.00000	0.99894
109 D	0.00106	0.00000	0.99894
110 A	0.00106	0.00000	0.99894
111 N	0.00106	0.00000	0.99894
112 G	0.00106	0.00000	0.99894
113 N	0.00106	0.00000	0.99894

114	I	0.00106	0.00000	0.99894
115	V	0.00106	0.00000	0.99894
116	Y	0.00106	0.00000	0.99894
117	E	0.00106	0.00000	0.99894
118	K	0.00106	0.00000	0.99894
119	N	0.00106	0.00000	0.99894
120	C	0.00106	0.00000	0.99894
121	R	0.00106	0.00000	0.99894
122	N	0.00106	0.00000	0.99894
123	E	0.00106	0.00000	0.99894
124	A	0.00106	0.00000	0.99894
125	G	0.00106	0.00000	0.99894
126	L	0.00106	0.00000	0.99894
127	S	0.00106	0.00000	0.99894
128	A	0.00106	0.00000	0.99894
129	D	0.00106	0.00000	0.99894
130	P	0.00106	0.00000	0.99894
131	Y	0.00106	0.00000	0.99894
132	V	0.00106	0.00000	0.99894
133	Y	0.00106	0.00000	0.99894
134	N	0.00106	0.00000	0.99894
135	W	0.00106	0.00000	0.99894
136	T	0.00106	0.00000	0.99894
137	A	0.00106	0.00000	0.99894
138	W	0.00106	0.00000	0.99894
139	S	0.00106	0.00000	0.99894
140	E	0.00106	0.00000	0.99894
141	D	0.00106	0.00000	0.99894
142	S	0.00106	0.00000	0.99894
143	D	0.00106	0.00000	0.99894
144	G	0.00106	0.00000	0.99894
145	E	0.00106	0.00000	0.99894
146	N	0.00106	0.00000	0.99894
147	G	0.00106	0.00000	0.99894
148	T	0.00106	0.00000	0.99894
149	G	0.00106	0.00000	0.99894
150	Q	0.00106	0.00000	0.99894
151	S	0.00106	0.00000	0.99894
152	H	0.00106	0.00000	0.99894
153	H	0.00106	0.00000	0.99894
154	N	0.00106	0.00000	0.99894
155	V	0.00106	0.00000	0.99894
156	F	0.00106	0.00000	0.99894
157	P	0.00106	0.00000	0.99894
158	D	0.00106	0.00000	0.99894
159	G	0.00106	0.00000	0.99894
160	K	0.00106	0.00000	0.99894
161	P	0.00106	0.00000	0.99894
162	F	0.00106	0.00000	0.99894
163	P	0.00106	0.00000	0.99894
164	H	0.00106	0.00000	0.99894
165	H	0.00106	0.00000	0.99894
166	P	0.00105	0.00000	0.99894
167	G	0.00105	0.00001	0.99894
168	W	0.00105	0.00001	0.99894
169	R	0.00105	0.00001	0.99894
170	R	0.00105	0.00001	0.99893
171	W	0.00105	0.00002	0.99893
172	N	0.00105	0.00002	0.99893
173	F	0.00105	0.00002	0.99893
174	I	0.00105	0.00002	0.99893
175	Y	0.00105	0.00002	0.99893
176	V	0.00105	0.00002	0.99893
177	F	0.00105	0.00002	0.99893
178	H	0.00105	0.00002	0.99893
179	T	0.00105	0.00002	0.99893
180	L	0.00105	0.00002	0.99893
181	G	0.00105	0.00002	0.99893
182	Q	0.00105	0.00002	0.99893
183	Y	0.00105	0.00002	0.99893
184	F	0.00105	0.00002	0.99893

185	Q	0.00106	0.00001	0.99893
186	K	0.00106	0.00001	0.99893
187	L	0.00106	0.00001	0.99893
188	G	0.00106	0.00000	0.99893
189	R	0.00106	0.00000	0.99893
190	C	0.00106	0.00000	0.99893
191	S	0.00106	0.00001	0.99893
192	V	0.00106	0.00001	0.99893
193	R	0.00106	0.00001	0.99893
194	V	0.00106	0.00001	0.99893
195	S	0.00106	0.00001	0.99893
196	V	0.00106	0.00001	0.99893
197	N	0.00106	0.00001	0.99893
198	T	0.00106	0.00001	0.99893
199	A	0.00106	0.00001	0.99893
200	N	0.00106	0.00001	0.99893
201	V	0.00106	0.00001	0.99893
202	T	0.00106	0.00001	0.99893
203	L	0.00106	0.00001	0.99893
204	G	0.00106	0.00001	0.99893
205	P	0.00106	0.00001	0.99893
206	Q	0.00106	0.00001	0.99893
207	L	0.00106	0.00001	0.99893
208	M	0.00106	0.00001	0.99893
209	E	0.00106	0.00001	0.99893
210	V	0.00106	0.00001	0.99893
211	T	0.00106	0.00001	0.99893
212	V	0.00106	0.00001	0.99893
213	Y	0.00106	0.00001	0.99893
214	R	0.00106	0.00000	0.99894
215	R	0.00106	0.00000	0.99894
216	H	0.00106	0.00000	0.99894
217	G	0.00106	0.00000	0.99894
218	R	0.00106	0.00000	0.99894
219	A	0.00106	0.00000	0.99894
220	Y	0.00106	0.00000	0.99894
221	V	0.00106	0.00001	0.99893
222	P	0.00106	0.00001	0.99893
223	I	0.00106	0.00001	0.99893
224	A	0.00106	0.00001	0.99893
225	Q	0.00106	0.00001	0.99893
226	V	0.00106	0.00001	0.99893
227	K	0.00106	0.00001	0.99893
228	D	0.00106	0.00001	0.99893
229	V	0.00106	0.00001	0.99893
230	Y	0.00106	0.00001	0.99893
231	V	0.00106	0.00001	0.99893
232	V	0.00106	0.00001	0.99893
233	T	0.00106	0.00001	0.99893
234	D	0.00106	0.00001	0.99893
235	Q	0.00106	0.00001	0.99893
236	I	0.00106	0.00001	0.99893
237	P	0.00106	0.00001	0.99893
238	V	0.00106	0.00001	0.99893
239	F	0.00106	0.00001	0.99893
240	V	0.00106	0.00001	0.99893
241	T	0.00106	0.00001	0.99893
242	M	0.00106	0.00000	0.99893
243	F	0.00106	0.00000	0.99893
244	Q	0.00106	0.00000	0.99894
245	K	0.00106	0.00000	0.99894
246	N	0.00106	0.00000	0.99894
247	D	0.00106	0.00000	0.99894
248	R	0.00106	0.00000	0.99894
249	N	0.00106	0.00000	0.99894
250	S	0.00106	0.00000	0.99894
251	S	0.00106	0.00000	0.99894
252	D	0.00106	0.00000	0.99894
253	E	0.00106	0.00000	0.99894
254	T	0.00106	0.00000	0.99894
255	F	0.00106	0.00000	0.99894




256	L	0.00106	0.00000	0.99894
257	K	0.00106	0.00000	0.99894
258	D	0.00106	0.00000	0.99894
259	L	0.00106	0.00000	0.99893
260	P	0.00106	0.00000	0.99893
261	I	0.00106	0.00000	0.99893
262	M	0.00106	0.00000	0.99893
263	F	0.00106	0.00000	0.99893
264	D	0.00106	0.00000	0.99893
265	V	0.00106	0.00000	0.99893
266	L	0.00106	0.00000	0.99893
267	I	0.00106	0.00000	0.99893
268	H	0.00106	0.00000	0.99893
269	D	0.00106	0.00000	0.99893
270	P	0.00106	0.00000	0.99893
271	S	0.00106	0.00000	0.99893
272	H	0.00106	0.00000	0.99893
273	F	0.00106	0.00000	0.99893
274	L	0.00106	0.00000	0.99893
275	N	0.00106	0.00000	0.99893
276	Y	0.00106	0.00000	0.99893
277	S	0.00106	0.00000	0.99893
278	T	0.00106	0.00000	0.99893
279	I	0.00106	0.00000	0.99893
280	N	0.00107	0.00000	0.99893
281	Y	0.00107	0.00000	0.99893
282	K	0.00107	0.00000	0.99893
283	W	0.00107	0.00000	0.99893
284	S	0.00107	0.00000	0.99893
285	F	0.00107	0.00001	0.99893
286	G	0.00107	0.00000	0.99893
287	D	0.00107	0.00000	0.99893
288	N	0.00107	0.00001	0.99893
289	T	0.00107	0.00001	0.99893
290	G	0.00107	0.00001	0.99892
291	L	0.00107	0.00001	0.99892
292	F	0.00107	0.00001	0.99892
293	V	0.00107	0.00001	0.99892
294	S	0.00107	0.00001	0.99892
295	T	0.00107	0.00001	0.99892
296	N	0.00107	0.00001	0.99892
297	H	0.00107	0.00001	0.99892
298	T	0.00107	0.00001	0.99892
299	V	0.00107	0.00001	0.99892
300	N	0.00107	0.00001	0.99892
301	H	0.00107	0.00001	0.99892
302	T	0.00107	0.00001	0.99892
303	Y	0.00107	0.00001	0.99892
304	V	0.00106	0.00001	0.99892
305	L	0.00107	0.00001	0.99892
306	N	0.00107	0.00001	0.99892
307	G	0.00107	0.00001	0.99892
308	T	0.00107	0.00001	0.99892
309	F	0.00107	0.00001	0.99892
310	S	0.00107	0.00001	0.99892
311	L	0.00107	0.00001	0.99892
312	N	0.00107	0.00001	0.99892
313	L	0.00107	0.00001	0.99892
314	T	0.00107	0.00000	0.99892
315	V	0.00107	0.00000	0.99892
316	K	0.00108	0.00000	0.99892
317	A	0.00108	0.00000	0.99892
318	A	0.00108	0.00000	0.99892
319	A	0.00108	0.00000	0.99892
320	P	0.00108	0.00000	0.99892
321	G	0.00108	0.00000	0.99892
322	P	0.00108	0.00000	0.99892
323	C	0.00108	0.00000	0.99892
324	P	0.00108	0.00000	0.99892
325	P	0.00108	0.00000	0.99892
326	P	0.00108	0.00000	0.99892

327	P	0.00108	0.00000	0.99892
328	P	0.00108	0.00000	0.99892
329	P	0.00108	0.00000	0.99892
330	P	0.00108	0.00000	0.99892
331	R	0.00108	0.00000	0.99892
332	P	0.00108	0.00000	0.99892
333	S	0.00108	0.00000	0.99892
334	K	0.00108	0.00000	0.99892
335	P	0.00108	0.00000	0.99892
336	T	0.00108	0.00000	0.99892
337	P	0.00108	0.00000	0.99892
338	S	0.00108	0.00000	0.99892
339	L	0.00108	0.00000	0.99892
340	G	0.00108	0.00000	0.99892
341	P	0.00108	0.00000	0.99892
342	A	0.00108	0.00000	0.99892
343	G	0.00108	0.00000	0.99892
344	D	0.00108	0.00000	0.99892
345	N	0.00108	0.00000	0.99892
346	P	0.00108	0.00000	0.99892
347	L	0.00108	0.00000	0.99892
348	E	0.00108	0.00000	0.99892
349	L	0.00108	0.00000	0.99892
350	S	0.00108	0.00000	0.99892
351	R	0.00108	0.00000	0.99892
352	I	0.00108	0.00000	0.99892
353	P	0.00108	0.00000	0.99892
354	D	0.00108	0.00000	0.99892
355	E	0.00108	0.00000	0.99892
356	N	0.00108	0.00000	0.99892
357	C	0.00108	0.00000	0.99892
358	Q	0.00108	0.00000	0.99892
359	I	0.00107	0.00001	0.99891
360	N	0.00107	0.00002	0.99891
361	R	0.00106	0.00003	0.99891
362	Y	0.00104	0.00013	0.99883
363	G	0.00104	0.00015	0.99881
364	H	0.00103	0.00017	0.99879
365	F	0.00103	0.00018	0.99879
366	Q	0.00102	0.00018	0.99879
367	A	0.00102	0.00019	0.99879
368	T	0.00102	0.00020	0.99879
369	I	0.00101	0.00020	0.99878
370	T	0.00101	0.00021	0.99878
371	I	0.00100	0.00021	0.99878
372	V	0.00100	0.00021	0.99878
373	E	0.00100	0.00021	0.99878
374	G	0.00100	0.00021	0.99878
375	I	0.00100	0.00021	0.99878
376	L	0.00100	0.00021	0.99878
377	E	0.00100	0.00021	0.99878
378	V	0.00100	0.00021	0.99878
379	N	0.00101	0.00021	0.99878
380	I	0.00101	0.00020	0.99878
381	I	0.00104	0.00018	0.99878
382	Q	0.00113	0.00007	0.99881
383	M	0.00113	0.00006	0.99881
384	T	0.00113	0.00005	0.99882
385	D	0.00114	0.00003	0.99884
386	V	0.00114	0.00003	0.99884
387	L	0.00114	0.00003	0.99884
388	M	0.00114	0.00002	0.99884
389	P	0.00114	0.00002	0.99885
390	V	0.00114	0.00002	0.99885
391	P	0.00114	0.00001	0.99885
392	W	0.00114	0.00001	0.99886
393	P	0.00114	0.00000	0.99886
394	E	0.00114	0.00000	0.99886
395	S	0.00114	0.00000	0.99885
396	S	0.00114	0.00001	0.99885
397	L	0.00114	0.00001	0.99885

398	I	0.00114	0.00001	0.99885
399	D	0.00114	0.00001	0.99885
400	F	0.00114	0.00001	0.99885
401	V	0.00114	0.00001	0.99885
402	V	0.00114	0.00001	0.99885
403	T	0.00114	0.00001	0.99885
404	C	0.00114	0.00001	0.99885
405	Q	0.00114	0.00001	0.99885
406	G	0.00114	0.00001	0.99885
407	S	0.00114	0.00001	0.99885
408	I	0.00114	0.00001	0.99885
409	P	0.00114	0.00001	0.99885
410	T	0.00114	0.00001	0.99885
411	E	0.00114	0.00001	0.99885
412	V	0.00114	0.00001	0.99885
413	C	0.00114	0.00001	0.99885
414	T	0.00114	0.00001	0.99885
415	I	0.00114	0.00001	0.99885
416	I	0.00114	0.00001	0.99885
417	S	0.00115	0.00000	0.99885
418	D	0.00115	0.00000	0.99885
419	P	0.00115	0.00000	0.99885
420	T	0.00115	0.00000	0.99885
421	C	0.00115	0.00000	0.99885
422	E	0.00115	0.00000	0.99885
423	I	0.00115	0.00000	0.99885
424	T	0.00115	0.00000	0.99885
425	Q	0.00115	0.00000	0.99885
426	N	0.00115	0.00000	0.99885
427	T	0.00115	0.00000	0.99885
428	V	0.00115	0.00000	0.99885
429	C	0.00115	0.00000	0.99885
430	S	0.00115	0.00000	0.99885
431	P	0.00115	0.00000	0.99885
432	V	0.00115	0.00000	0.99885
433	D	0.00115	0.00000	0.99885
434	V	0.00115	0.00000	0.99885
435	D	0.00115	0.00000	0.99885
436	E	0.00115	0.00000	0.99885
437	M	0.00115	0.00000	0.99885
438	C	0.00115	0.00000	0.99885
439	L	0.00115	0.00000	0.99885
440	L	0.00115	0.00000	0.99885
441	T	0.00115	0.00000	0.99885
442	V	0.00115	0.00000	0.99885
443	R	0.00115	0.00000	0.99885
444	R	0.00115	0.00000	0.99885
445	T	0.00114	0.00001	0.99884
446	F	0.00113	0.00002	0.99884
447	N	0.00113	0.00003	0.99884
448	G	0.00112	0.00005	0.99884
449	S	0.00111	0.00006	0.99883
450	G	0.00109	0.00011	0.99881
451	T	0.00092	0.00030	0.99877
452	Y	0.00074	0.00050	0.99876
453	C	0.00072	0.00053	0.99876
454	V	0.00070	0.00055	0.99875
455	N	0.00070	0.00055	0.99875
456	L	0.00070	0.00056	0.99874
457	T	0.00070	0.00056	0.99874
458	L	0.00070	0.00056	0.99874
459	G	0.00070	0.00056	0.99874
460	D	0.00070	0.00056	0.99874
461	D	0.00070	0.00056	0.99874
462	T	0.00070	0.00056	0.99874
463	S	0.00070	0.00056	0.99874
464	L	0.00070	0.00056	0.99874
465	A	0.00070	0.00055	0.99875
466	L	0.00070	0.00055	0.99875
467	T	0.00071	0.00055	0.99875
468	S	0.00071	0.00054	0.99875

469 T	0.00071	0.00053	0.99876
470 L	0.00071	0.00052	0.99877
471 I	0.00071	0.00050	0.99879
472 S	0.00072	0.00047	0.99882
473 V	0.00075	0.00041	0.99884
474 P	0.00080	0.00017	0.99903
475 D	0.00081	0.00001	0.99919
476 R	0.00081	0.00000	0.99919
477 D	0.00081	0.00000	0.99919
478 P	0.00081	0.00001	0.99918
479 A	0.00081	0.00024	0.99895
480 S	0.00081	0.00065	0.99853
481 P	0.00081	0.00126	0.99793
482 L	0.00081	0.00527	0.99391
483 R	0.00080	0.01342	0.98577
484 M	0.00072	0.23647	0.76281
485 A	0.00030	0.54536	0.45434
486 N	0.00025	0.58448	0.41528
487 S	0.00018	0.68094	0.31887
488 A	0.00007	0.91632	0.08361
489 L	0.00001	0.98533	0.01466
490 I	0.00000	0.99200	0.008
491 S	0.00000	0.99227	0.00772
492 V	0.00000	0.99245	0.00755
493 G	0.00000	0.99247	0.00753
494 C	0.00000	0.99247	0.00753
495 L	0.00000	0.99247	0.00753
496 A	0.00000	0.99247	0.00753
497 I	0.00000	0.99247	0.00753
498 F	0.00000	0.99247	0.00753
499 V	0.00000	0.99247	0.00753
500 T	0.00003	0.99244	0.00753
501 V	0.00004	0.99243	0.00753
502 I	0.00048	0.99199	0.00753
503 S	0.00161	0.99085	0.00753
504 L	0.00325	0.98921	0.00754
505 L	0.01311	0.97933	0.00756
506 V	0.05549	0.93691	0.0076
507 Y	0.41061	0.58161	0.00778
508 K	0.96651	0.02517	0.00832
509 K	0.98966	0.00200	0.00834
510 H	0.99112	0.00054	0.00834
511 K	0.99165	0.00001	0.00834
512 E	0.99166	0.00000	0.00834
513 Y	0.99166	0.00000	0.00834
514 N	0.99166	0.00000	0.00834
515 P	0.99166	0.00000	0.00834
516 I	0.99166	0.00000	0.00834
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518 N	0.99166	0.00000	0.00834
519 S	0.99165	0.00001	0.00834
520 P	0.99165	0.00001	0.00834
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523 V	0.99163	0.00003	0.00834
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527 K	0.99161	0.00005	0.00834
528 G	0.99155	0.00011	0.00834
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540 F 0.99155	0.00011	0.00834
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559 V 0.99155	0.00000	0.00845
560 S 0.99155	0.00000	0.00845

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Bio

Search **Protein** for **Go** **Clear**

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☐ 1: P02786. Transferrin recep...[gi:136378]

[BLink](#), [Domains](#), [Links](#)

LOCUS P02786 760 aa linear PRI 15-SEP-2003
 DEFINITION Transferrin receptor protein 1 (TFR1) (TR) (TfR) (Trfr) (CD71 antigen) (T9) (p90).
 ACCESSION P02786
 VERSION P02786 GI:136378
 DBSOURCE swissprot: locus TFR1_HUMAN, accession P02786;
 class: standard.
 extra accessions: Q9UCN0, Q9UCU5, Q9UDF9, Q9UK21, created: Jul 21, 1986.
 sequence updated: Jul 21, 1986.
 annotation updated: Sep 15, 2003.
 xrefs: gi: 37432, gi: 37433, gi: 339515, gi: 339516, gi: 6164847, gi: 6164848, gi: 12654696, gi: 12654697, gi: 72139, pdb accession 1CX8, pdb accession 1DE4
 xrefs (non-sequence databases): MEROPSM28.972, GlycoSuiteDBP02786, GeneHGNC:11763, MIM 190010, GOGO:0005768, GOGO:0005576, GOGO:0005887, GOGO:0004998, GOGO:0006879, InterProIPR003137, PfamPF02225, PfamPF04389, PfamPF04253

KEYWORDS Transmembrane; Glycoprotein; Receptor; Lipoprotein; Palmitate; Signal-anchor; Endocytosis; Phosphorylation; Polymorphism; 3D-structure.

SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (residues 1 to 760)
AUTHORS Schneider, C., Owen, M.J., Banville, D. and Williams, J.G.
TITLE Primary structure of human transferrin receptor deduced from the mRNA sequence
JOURNAL Nature 311 (5987), 675-678 (1984)
MEDLINE 85012743
REMARK SEQUENCE FROM N.A.

REFERENCE 2 (residues 1 to 760)
AUTHORS McClelland, A., Kuhn, L.C. and Ruddie, F.H.
TITLE The human transferrin receptor gene: genomic organization, and the complete primary structure of the receptor deduced from a cDNA sequence
JOURNAL Cell 39 (2 Pt 1), 267-274 (1984)
MEDLINE 85048936
REMARK SEQUENCE FROM N.A.

REFERENCE 3 (residues 1 to 760)
AUTHORS Evans, P. and Kemp, J.
TITLE Exon/intron structure of the human transferrin receptor gene
JOURNAL Gene 199 (1-2), 123-131 (1997)
MEDLINE 98019079
REMARK SEQUENCE FROM N.A.
 TISSUE=Placenta

REFERENCE 4 (residues 1 to 760)

AUTHORS Wheeler,D.L.
 TITLE Molecular and evolutionary studies of the transferrin receptor
 JOURNAL Thesis (1999)
 REMARK SEQUENCE FROM N.A.
 TISSUE=Placenta

REFERENCE 5 (residues 1 to 760)
 AUTHORS Strausberg,R.L., Feingold,E.A., Grouse,L.H., Derge,J.G., Klausner,R.D., Collins,F.S., Wagner,L., Shenmen,C.M., Schuler,G.D., Altschul,S.F., Zeeberg,B., Buetow,K.H., Schaefer,C.F., Bhat,N.K., Hopkins,R.F., Jordan,H., Moore,T., Max,S.I., Wang,J., Hsieh,F., Diatchenko,L., Marusina,K., Farmer,A.A., Rubin,G.M., Hong,L., Stapleton,M., Soares,M.B., Bonaldo,M.F., Casavant,T.L., Scheetz,T.E., Brownstein,M.J., Usdin,T.B., Toshiyuki,S., Carninci,P., Prange,C., Raha,S.S., Loquellano,N.A., Peters,G.J., Abramson,R.D., Mullahy,S.J., Bosak,S.A., McEwan,P.J., McKernan,K.J., Malek,J.A., Gunaratne,P.H., Richards,S., Worley,K.C., Hale,S., Garcia,A.M., Gay,L.J., Hulyk,S.W., Villalon,D.K., Muzny,D.M., Sodergren,E.J., Lu,X., Gibbs,R.A., Fahey,J., Helton,E., Kettelman,M., Madan,A., Rodrigues,S., Sanchez,A., Whiting,M., Madan,A., Young,A.C., Shevchenko,Y., Bouffard,G.G., Blakesley,R.W., Touchman,J.W., Green,E.D., Dickson,M.C., Rodriguez,A.C., Grimwood,J., Schmutz,J., Myers,R.M., Butterfield,Y.S.N., Krzywinski,M.I., Skalska,U., Smailus,D.E., Schnerch,A., Schein,J.E., Jones,S.J.M. and Marra,M.A.

TITLE Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (26), 16899-16903 (2002)
 MEDLINE 22388257
 REMARK SEQUENCE FROM N.A.
 TISSUE=Eye

REFERENCE 6 (residues 1 to 760)
 AUTHORS Shih,Y.J., Baynes,R.D., Hudson,B.G., Flowers,C.H., Skikne,B.S. and Cook,J.D.

TITLE Serum transferrin receptor is a truncated form of tissue receptor
 JOURNAL J. Biol. Chem. 265 (31), 19077-19081 (1990)
 MEDLINE 91035436
 REMARK SEQUENCE OF 101-119 (STFR).

REFERENCE 7 (residues 1 to 760)
 AUTHORS Baynes,R.D., Shih,Y.J., Hudson,B.G. and Cook,J.D.

TITLE Characterization of transferrin receptor released by K562 erythroleukemia cells
 JOURNAL Proc Soc Exp Biol Med 197 (4), 416-423 (1991)
 MEDLINE 91334496
 REMARK SEQUENCE OF 101-123 (STFR), AND CHARACTERIZATION.
 TISSUE=Erythroleukemia

REFERENCE 8 (residues 1 to 760)
 AUTHORS Coppolino,M., Migliorini,M., Argraves,W.S. and Dedhar,S.

TITLE Identification of a novel form of the alpha 3 integrin subunit: covalent association with transferrin receptor
 JOURNAL Biochem. J. 306 (Pt 1), 129-134 (1995)
 MEDLINE 95169043
 REMARK SEQUENCE OF 288-302; 694-708 AND 721-730.
 TISSUE=Prostatic carcinoma

REFERENCE 9 (residues 1 to 760)
 AUTHORS Chiciz,R.M., Urban,R.G., Lane,W.S., Gorga,J.C., Stern,L.J., Vignali,D.A. and Strominger,J.L.

TITLE Predominant naturally processed peptides bound to HLA-DRI are derived from MHC-related molecules and are heterogeneous in size
 JOURNAL Nature 358 (6389), 764-768 (1992)
 MEDLINE 92375195

REMARK SEQUENCE OF 680-696.
REFERENCE 10 (residues 1 to 760)
AUTHORS Jing,S.Q. and Trowbridge,I.S.
TITLE Identification of the intermolecular disulfide bonds of the human transferrin receptor and its lipid-attachment site
JOURNAL EMBO J. 6 (2), 327-331 (1987)
MEDLINE 87218484
REMARK PALMITOYLATION OF CYS-62.
REFERENCE 11 (residues 1 to 760)
AUTHORS Alvarez,E., Girones,N. and Davis,R.J.
TITLE Intermolecular disulfide bonds are not required for the expression of the dimeric state and functional activity of the transferrin receptor
JOURNAL EMBO J. 8 (8), 2231-2240 (1989)
MEDLINE 90005427
REMARK MUTAGENESIS OF CYSTEINES INVOLVED IN INTERMOLECULAR BONDS.
REFERENCE 12 (residues 1 to 760)
AUTHORS Jing,S.Q., Spencer,T., Miller,K., Hopkins,C. and Trowbridge,I.S.
TITLE Role of the human transferrin receptor cytoplasmic domain in endocytosis: localization of a specific signal sequence for internalization
JOURNAL J. Cell Biol. 110 (2), 283-294 (1990)
MEDLINE 90130619
REMARK INTERNALIZATION SEQUENCE, AND MUTAGENESIS OF TYR-20.
REFERENCE 13 (residues 1 to 760)
AUTHORS Do,S.I. and Cummings,R.D.
TITLE Presence of O-linked oligosaccharide on a threonine residue in the human transferrin receptor
JOURNAL Glycobiology 2 (4), 345-353 (1992)
MEDLINE 93043836
REMARK CARBOHYDRATE-LINKAGE SITES THR-104.
REFERENCE 14 (residues 1 to 760)
AUTHORS Hayes,G.R., Enns,C.A. and Lucas,J.J.
TITLE Identification of the O-linked glycosylation site of the human transferrin receptor
JOURNAL Glycobiology 2 (4), 355-359 (1992)
MEDLINE 93043837
REMARK CARBOHYDRATE-LINKAGE SITES THR-104.
REFERENCE 15 (residues 1 to 760)
AUTHORS Hayes,G.R., Williams,A., Costello,C.E., Enns,C.A. and Lucas,J.J.
TITLE The critical glycosylation site of human transferrin receptor contains a high-mannose oligosaccharide
JOURNAL Glycobiology 5 (2), 227-232 (1995)
MEDLINE 95299226
REMARK STRUCTURE OF CARBOHYDRATES ON ASN-727.
REFERENCE 16 (residues 1 to 760)
AUTHORS Buchegger,F., Trowbridge,I.S., Liu,L.F., White,S. and Collawn,J.F.
TITLE The critical glycosylation site of human transferrin receptor chimeras indicates that the carboxy-terminal region is important for ligand binding
JOURNAL Eur. J. Biochem. 235 (1-2), 9-17 (1996)
MEDLINE 96202913
REMARK IDENTIFICATION OF LIGAND BINDING DOMAIN.
REFERENCE 17 (residues 1 to 760)
AUTHORS Collawn,J.F., Lai,A., Domingo,D., Fitch,M., Hatton,S. and Trowbridge,I.S.
TITLE YTRF is the conserved internalization signal of the transferrin receptor, and a second YTRF signal at position 31-34 enhances endocytosis
JOURNAL J. Biol. Chem. 268 (29), 21686-21692 (1993)

MEDLINE 94012749
REMARK MUTAGENESIS OF ENDOCYTOSIS SITE.
REFERENCE 18 (residues 1 to 760)
AUTHORS Alvarez,E., Girones,N. and Davis,R.J.
TITLE A point mutation in the cytoplasmic domain of the transferrin receptor inhibits endocytosis
JOURNAL Biochem. J. 267 (1), 31-35 (1990)
MEDLINE 90226333
REMARK MUTAGENESIS OF TYR-20.
REFERENCE 19 (residues 1 to 760)
AUTHORS Dubljevic,V., Sali,A. and Goding,J.W.
TITLE A conserved RGD (Arg-Gly-Asp) motif in the transferrin receptor is required for binding to transferrin
JOURNAL Biochem. J. 341 (Pt 1), 11-14 (1999)
MEDLINE 99306849
REMARK MUTAGENESIS OF RGD MOTIF.
REFERENCE 20 (residues 1 to 760)
AUTHORS West,A.P. Jr., Giannetti,A.M., Herr,A.B., Bennett,M.J., Nangiana,J.S., Pierce,J.R., Weiner,L.P., Snow,P.M. and Bjorkman,P.J.
TITLE Mutational analysis of the transferrin receptor reveals overlapping HFE and transferrin binding sites
JOURNAL J. Mol. Biol. 313 (2), 385-397 (2001)
MEDLINE 21659940
REMARK MUTAGENESIS.
REFERENCE 21 (residues 1 to 760)
AUTHORS Fuchs,H., Lucken,U., Tauber,R., Engel,A. and Gessner,R.
TITLE Structural model of phospholipid-reconstituted human transferrin receptor derived by electron microscopy
JOURNAL Structure 6 (10), 1235-1243 (1998)
MEDLINE 98455506
REMARK ELECTRON MICROSCOPY.
REFERENCE 22 (residues 1 to 760)
AUTHORS Lawrence,C.M., Ray,S., Babyonyshev,M., Galluser,R., Borhani,D.W. and Harrison,S.C.
TITLE Crystal structure of the ectodomain of human transferrin receptor
JOURNAL Science 286 (5440), 779-782 (1999)
MEDLINE 20002984
REMARK X-RAY CRYSTALLOGRAPHY (3.2 ANGSTROMS) OF 121-760.
REFERENCE 23 (residues 1 to 760)
AUTHORS Douabin-Gicquel,V., Soriano,N., Ferran,H., Wojcik,F., Palierne,E., Tamim,S., Jovelin,T., McKie,A.T., Le Gall,J.-Y., David,V. and Mosser,J.
TITLE Identification of 96 single nucleotide polymorphisms in eight genes involved in iron metabolism: efficiency of bioinformatic extraction compared with a systematic sequencing approach
JOURNAL Hum. Genet. 109 (4), 393-401 (2001)
MEDLINE 21558434
REMARK VARIANT GLY-142.
COMMENT

This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and the EMBL outstation - the European Bioinformatics Institute. The original entry is available from <http://www.expasy.ch/sprot> and <http://www.ebi.ac.uk/sprot>

[FUNCTION] Cellular uptake of iron occurs via receptor-mediated endocytosis of ligand-occupied transferrin receptor into specialized endosomes. Endosomal acidification leads to iron release. The apotransferrin-receptor complex is then recycled to

the cell surface with a return to neutral pH and the concomitant loss of affinity of apotransferrin for its receptor. Transferrin receptor is necessary for development of erythrocytes and the nervous system (By similarity). A second ligand, the hereditary hemochromatosis protein HFE, competes for binding with transferrin for an overlapping C-terminal binding site.

[SUBUNIT] Homodimer; disulfide-linked. Binds one transferrin or HFE molecule per polypeptide chain. Binds the HLA class II histocompatibility antigen, DR1.

[SUBCELLULAR LOCATION] Type II membrane protein. The sTfr isoform is secreted.

[INDUCTION] Regulated by cellular iron levels through binding of the iron regulatory proteins, IRP1 and IRP2, to iron-responsive elements in the 3'-UTR. Up-regulated upon mitogenic stimulation.

[PTM] N- and O-glycosylated, phosphorylated and palmitoylated. The serum form is only glycosylated.

[PTM] Proteolytically cleaved on Arg-100 to produce the soluble serum form (sTfr).

[MISCELLANEOUS] Serum transferrin receptor (sTfr) is used as a means of detecting erythropoietin (EPO) misuse by athletes and as a diagnostic test for anemias resulting from a number of conditions including rheumatoid arthritis, pregnancy, irritable bowel syndrome and in HIV patients.

[MISCELLANEOUS] Canine and feline parvoviruses bind human and feline transferrin receptors and use these receptors to enter and infect cells.

[SIMILARITY] BELONGS TO PEPTIDASE FAMILY M28B.

[DATABASE] NAME=PROW; NOTE=CD guide CD71 entry;

WWW='http://www.ncbi.nlm.nih.gov/prow/cd/cd71.htm'.

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<u>gene</u>	1..760 /gene="TFRC"
<u>Protein</u>	1..760 /gene="TFRC" /product="Transferrin receptor protein 1"
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<u>Site</u>	9..12 /gene="TFRC" /site_type="mutagenized" /note="FSNL->YTRF: ONLY 80 % AS ACTIVE AS WILD-TYPE RECEPTOR. UPTAKE OF THE RECEPTOR."
<u>Site</u>	20..34 /gene="TFRC" /site_type="mutagenized" /note="YTRFSLARQVDGNS->PPGYSLARQVDYTRF: NO INFLUENCE ON ENDOCYTIC UPTAKE OF THE RECEPTOR."
<u>Site</u>	20..23 /gene="TFRC" /site_type="mutagenized" /note="YTRF->PPGY: ONLY 16% AS ACTIVE AS WILD-TYPE RECEPTOR."
<u>Site</u>	20..23 /gene="TFRC" /site_type="unclassified"


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Site      /note="Y->G: ONLY 20% AS ACTIVE AS WILD-TYPE RECEPTOR."
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Site      /note="T->TA: ONLY 14% AS ACTIVE AS WILD-TYPE RECEPTOR."
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Site      /note="T->F: ONLY 88% AS ACTIVE AS WILD-TYPE RECEPTOR."
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/gene="TFRC"
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Site      /note="F->Y: ONLY 48% AS ACTIVE AS WILD-TYPE RECEPTOR."
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/site_type="phosphorylation"
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OF THE RECEPTOR."
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RECEPTOR. NO BINDING TO HFE."
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/site_type="mutagenized"
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721 qnngafnetl frnqlalatw tiqqaanals gdwvwdidnef

//

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May 20 2003 11:20:12



1: Q9UP52. Transferrin recep...[gi:21040912]

BLink, Domains, Links

LOCUS Q9UP52 801 aa linear PRI 15-SEP-2003
 DEFINITION Transferrin receptor protein 2 (TfR2).
 ACCESSION Q9UP52
 VERSION Q9UP52 GI:21040912
 DBSOURCE swissprot: locus TFR2_HUMAN, accession Q9UP52;
 class: standard.
 extra accessions: O75422, Q9HA99, Q9NX67, created: Feb 28, 2003.
 sequence updated: Feb 28, 2003.
 annotation updated: Sep 15, 2003.
 xrefs: gi: 5596369, gi: 5596370, gi: 3135305, gi: 3135312, gi: 10433313, gi: 10433314, gi: 7020497, gi: 7020498
 xrefs (non-sequence databases): HSSPP02786, MEROPSM28.973, GenewHGNC:11762, MIM 604720, MIM 604250, GOGO:0005887, GOGO:0004998, GOGO:0006826, InterProIPR003137, PfamPF04225, PfamPF04389, PfamPF04253
 KEYWORDS Transmembrane; Glycoprotein; Receptor; Signal-anchor; Alternative splicing; Disease mutation.
 SOURCE Homo sapiens (human)
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (residues 1 to 801)
 AUTHORS Kawabata, H., Yang, R., Hirama, T., Vuong, P.T., Kawano, S., Gombart, A.F. and Koeffler, H.P.
 TITLE Molecular cloning of transferrin receptor 2. A new member of the transferrin receptor-like family
 JOURNAL J. Biol. Chem. 274 (30), 20826-20832 (1999)
 MEDLINE 99340005
 PUBMED 10409623
 REMARK SEQUENCE FROM N.A. (ISOFORMS ALPHA AND BETA).
 TISSUE=Erythroleukemia, and Myeloid leukemia cells
 REFERENCE 2 (residues 1 to 801)
 AUTHORS Glockner, G., Scherer, S., Schattevoy, R., Boright, A., Weber, J., Tsui, L.C. and Rosenthal, A.
 TITLE Large-scale sequencing of two regions in human chromosome 7q22: analysis of 650 kb of genomic sequence around the EPO and CUTL1 loci reveals 17 genes
 JOURNAL Genome Res. 8 (10), 1060-1073 (1998)
 MEDLINE 99018118
 PUBMED 9799793
 REMARK SEQUENCE FROM N.A. (ISOFORM GAMMA).
 REFERENCE 3 (residues 1 to 801)
 AUTHORS Isogai, T., Ota, T., Hayashi, K., Sugiyama, T., Otsuki, T., Suzuki, Y., Nishikawa, T., Nagai, K., Sugano, S., Shiratori, A., Sudo, H., Wagatsuma, M., Hosoi, T., Kaku, Y., Kodaira, H., Kondo, H., Sugawara, M., Takahashi, M., Chiba, Y., Ishida, S., Murakawa, K., Ono, Y., Takiguchi, S., Watanabe, S., Kimura, K., Murakami, K.,

Ishii,S., Kawai,Y., Saito,K., Yamamoto,J., Wakamatsu,A.,
 Nakamura,Y., Nagahari,K., Masuho,Y., Ninomiya,K. and Iwayanagi,T.
 TITLE Direct Submission
 JOURNAL Submitted (~AUG-2000)
 REMARK SEQUENCE OF 1-158 AND 370-801 FROM N.A.
 TISSUE=Carcinoma, and Embryo
 REFERENCE 4 (residues 1 to 801)
 AUTHORS Camaschella,C., Roetto,A., Cali,A., De Gobbi,M., Garozzo,G.,
 Carella,M., Majorano,N., Totaro,A. and Gasparini,P.
 TITLE The gene TFR2 is mutated in a new type of haemochromatosis mapping
 to 7q22
 JOURNAL Nat. Genet. 25 (1), 14-15 (2000)
 MEDLINE 20264357
 PUBMED 10802645
 REMARK DISEASE.
 REFERENCE 5 (residues 1 to 801)
 AUTHORS Roetto,A., Totaro,A., Piperno,A., Piga,A., Longo,F., Garozzo,G.,
 Cali,A., De Gobbi,M., Gasparini,P. and Camaschella,C.
 TITLE New mutations inactivating transferrin receptor 2 in
 hemochromatosis type 3
 JOURNAL Blood 97 (9), 2555-2560 (2001)
 MEDLINE 21213521
 PUBMED 11313241
 REMARK VARIANT HFE3 LYS-172.
 COMMENT

 This SWISS-PROT entry is copyright. It is produced through a
 collaboration between the Swiss Institute of Bioinformatics and
 the EMBL outstation - the European Bioinformatics Institute.
 The original entry is available from <http://www.expasy.ch/sprot>
 and <http://www.ebi.ac.uk/sprot>

[FUNCTION] Mediates cellular uptake of transferrin-bound iron in a
 non-iron dependent manner. May be involved in iron metabolism,
 hepatocyte function and erythrocyte differentiation.
 [SUBUNIT] Homodimer.
 [SUBCELLULAR LOCATION] Type II membrane protein. The beta isoform
 lacks the transmembrane domain and is probably intracellular.
 [ALTERNATIVE PRODUCTS] Event=Alternative splicing; Named
 isoforms=3; Name=Alpha; IsoId=Q9UP52-1; Sequence=Displayed;
 Name=Beta; IsoId=Q9UP52-2; Sequence=VSP_005354; Name=Gamma;
 IsoId=Q9UP52-3; Sequence=VSP_005355.
 [TISSUE SPECIFICITY] Predominantly expressed in liver. While the
 alpha form is also expressed in spleen, lung, muscle, prostate and
 peripheral blood mononuclear cells, the beta form is expressed in
 all tissues tested, albeit weakly.
 [DISEASE] Defects in TFR2 are a cause of hereditary hemochromatosis
 type 3 (HFE3) [MIM:604250]. HFE3 is a disorder of iron homeostasis
 resulting in iron overload and has a phenotype indistinguishable
 from that of hereditary hemochromatosis (HH). HH is characterized
 by abnormal intestinal iron absorption and progressive increase of
 total body iron, which results in midlife in clinical complications
 including cirrhosis, cardiopathy, diabetes, endocrine dysfunctions,
 arthropathy, and susceptibility to liver cancer. Since the disease
 complications can be effectively prevented by regular phlebotomies,
 early diagnosis is most important to provide a normal life
 expectancy to the affected subjects.
 [MISCELLANEOUS] The variant lys-172 found in hereditary
 hemochromatosis type III affects the putative initiation codon of
 the beta isoform thus preventing its translation.
 [SIMILARITY] BELONGS TO PEPTIDASE FAMILY M28B.

FEATURES . Location/Qualifiers

source 1..801
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/db_xref="taxon:9606"

gene 1..801
/gene="TFR2"

Protein 1..801
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/product="Transferrin receptor protein 2"

Region 1..171
/gene="TFR2"
/region_name="Splicing variant"
/note="Missing (in isoform Beta). /FTId=VSP_005354."

Region 1..83
/gene="TFR2"
/region_name="Domain"
/note="CYTOPLASMIC (POTENTIAL)."

Site 23..26
/gene="TFR2"
/site_type="unclassified"
/note="ENDOCYTOSIS SIGNAL (POTENTIAL)."

Region 84..104
/gene="TFR2"
/region_name="Transmembrane region"
/note="SIGNAL-ANCHOR (TYPE-II MEMBRANE PROTEIN) (POTENTIAL)."

Region 105..801
/gene="TFR2"
/region_name="Domain"
/note="EXTRACELLULAR (POTENTIAL)."

Bond bond(108)
/gene="TFR2"
/bond_type="disulfide"
/note="INTERCHAIN (POTENTIAL)."

Bond bond(111)
/gene="TFR2"
/bond_type="disulfide"
/note="INTERCHAIN (POTENTIAL)."

Region 172
/gene="TFR2"
/region_name="Variant"
/note="M -> K (IN HFE3). /FTId=VAR_012738."

Site 240
/gene="TFR2"
/site_type="glycosylation"
/note="N-LINKED (GLCNAC...) (POTENTIAL)."

Site 339
/gene="TFR2"
/site_type="glycosylation"
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Region 343..369
/gene="TFR2"
/region_name="Splicing variant"
/note="Missing (in isoform Gamma). /FTId=VSP_005355."

Site 540
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Region 712
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Site

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/region_name="Conflict"  
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754  
/gene="TFR2"  
/site_type="glycosylation"  
/note="N-LINKED (GLCNAC...) (POTENTIAL)."
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ORIGIN

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1 merlwglfqr aqqlsprssq tvyqrvegpr kghleeeed geegaetlah fcpmelrgpe  
61 plgsrprqpn lipwaaagrr aapylvltal liftgaflig yvafrgscqa cgdsvlvvse  
121 dvnypdlidf hqgrlywsdl qamflqlfge grledtirqt slrervagsa gmaaltqdir  
181 aalsrqkldh vwtldthyvgl qfdpdphnt lhwvdeagkv geqlpledps vycpysain  
241 vtgelvyahy grpedlqdlr argvdpvgrl llvrvgvisf aqkvtnaqdf gaqgvliype  
301 padfsgdppk pslssqgavy ghvhlgtgdp ytpgfpsfnq tqfppvassg lpsipaqpis  
361 adiasrlrrk lkgpvapgew qgsllgspyh lggprlrlv vnnhrtstpi nnifgciegr  
421 sepdhyvvig aqrdawgpga aksavgtail lelvrftfsm vsngfrprsr llfiswdggd  
481 fgsvgstewl egylsvlhik avvysldna vlgddkfhak tsplltslie svlkqvdsnp  
541 hsgqtlyeqv vftnpswdae virplpmdss aysftafvgv pavefsmed dqaypflhtk  
601 edtyenlhkv lqgrlpavaq avaqlagqll irlshdrllp ldgrygddv lrhignlnef  
661 sgdlkarglt lqwyysargd yiraaeklrr eiysseerde rltmynvri mrveyfllsq  
721 yvspadspfr hifmgrgdht lgalldhlrl lrsnssgtpg atsstgfqes rfrrqlallt  
781 wtlqgaanal sgdvwnidnn f
```

//

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Blast 2 Sequences results

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BLAST

OMIM

Taxonomy

Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.5 [Nov-16-2002]

Matrix: BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.0001 wordsize: 3 Filter ☐ Align ☐

Sequence 1 lcl|seq_1 Length 560

GPNMB

X76534

Sequence 2 lcl|seq_2 Length 760

Transferin Receptor 1

P02786

No significant similarity was found



Blast 2 Sequences results

PubMed

Entrez

BLAST

OMIM

Taxonomy

Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.5 [Nov-16-2002]

Matrix: BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.000 wordsize: 3 Filter ☐ Align ☐

Sequence 1 lc|seq_1 Length 560

GPNMB

Y76534

Sequence 2 lc|seq_2 Length 801

Transferrin Receptor Protein 2 Q94P52

No significant similarity was found



☐ PubMed
 ☐ Nucleotide
 ☒ Protein
 ☐ Genome
 ☐ Structure
 ☐ PMC
 ☐ Taxonomy
 ☐ OMIM
 ☐ Bio

Search for

Display Show:

1: NP_066563. neuromedin B [Hom...[gi:10835107]

BLink, Links

LOCUS NMB 121 aa linear PRI 06-APR-2003
 DEFINITION neuromedin B [Homo sapiens].
 ACCESSION NP_066563
 VERSION NP_066563.1 GI:10835107
 DBSOURCE REFSEQ: accession NM_021077.2
 KEYWORDS .
 SOURCE Homo sapiens (human)
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (residues 1 to 121)
 AUTHORS Richard, I., Broux, O., Chiannilkulchai, N., Fougerousse, F.,
 Allamand, V., Bourg, N., Brenguier, L., Devaud, C., Pasturaud, P.,
 Roudaut, C. et al.
 TITLE Regional localization of human chromosome 15 loci
 JOURNAL Genomics 23 (3), 619-627 (1994)
 MEDLINE 95154832
 PUBMED 7851890
 REFERENCE 2 (residues 1 to 121)
 AUTHORS Krane, I.M., Naylor, S.L., Helin-Davis, D., Chin, W.W. and Spindel, E.R.
 TITLE Molecular cloning of cDNAs encoding the human bombesin-like peptide
 neuromedin B. Chromosomal localization and comparison to cDNAs
 encoding its amphibian homolog ranatensin
 J. Biol. Chem. 263 (26), 13317-13323 (1988)
 JOURNAL
 MEDLINE 88330837
 PUBMED 2458345
 COMMENT PROVISIONAL REFSEQ: This record has not yet been subject to final
 NCBI review. The reference sequence was derived from M21551.1.
 FEATURES
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 /organism="Homo sapiens"
 /db_xref="taxon:9606"
 /chromosome="15"
 /map="15q22-qter"
 /tissue_type="hypothalamus"
 /tissue_lib="of R.Goodman"
Protein 1..121
 /product="neuromedin B"
sig_peptide 1..24
 /gene="NMB"
 /note="G00-120-237"
mat_peptide 25..57
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CDS 1..121
 /gene="NMB"

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/coded_by="NM_021077.2:37..402"  
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ORIGIN

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1 marraggarm fgslllfall aagvaplswd lpeprsrask irvhsrgnlw atghfmgkks  
61 lepsspshwg qltpplrdq rlglsdillg illlkkalgv slsrpapiq yrrllvqilq  
121 k
```

//

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Mar 17 2003 10:55:57



PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Bio
 Search for
 Limits Preview/Index History Clipboard Details
 Display Show: Send to Get Subsequence

☐ 1: NP_002501. glycoprotein (tra...[gi:4505405]

[BLink](#), [Domains](#), [Links](#)

LOCUS GPNMB 560 aa linear PRI 05-APR-2003
 DEFINITION glycoprotein (transmembrane) nmb; transmembrane glycoprotein [Homo sapiens].
 ACCESSION NP_002501
 VERSION NP_002501.1 GI:4505405
 DBSOURCE REFSEQ: accession [NM_002510.1](#)
 KEYWORDS
 SOURCE Homo sapiens (human)
 ORGANISM [Homo sapiens](#)
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (residues 1 to 560)
 AUTHORS Weterman,M.A., Ajubi,N., van Dinter,I.M., Degen,W.G., van Muijen,G.N., Rutter,D.J. and Bloemers,H.P.
 TITLE nmb, a novel gene, is expressed in low-metastatic human melanoma cell lines and xenografts
 JOURNAL Int. J. Cancer 60 (1), 73-81 (1995)
 MEDLINE [95113576](#)
 PUBMED [7814155](#)
 COMMENT REVIEWED [REFSEQ](#): This record has been curated by NCBI staff. The reference sequence was derived from [X76534.1](#).

Summary: GPNMB is a transmembrane glycoprotein which shows homology to the pMEL17 precursor, a melanocyte-specific protein. GPNMB shows expression in the lowly metastatic human melanoma cell lines and xenografts but does not show expression in the highly metastatic cell lines; although, it is also expressed in other tissues and tumor cell lines as well. GPNMB may be involved in growth delay and reduction of metastatic potential.

FEATURES Location/Qualifiers
 source 1..560
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 /db_xref="taxon:9606"
 /chromosome="7"
 /map="7p15"
 Protein 1..560
 /product="glycoprotein (transmembrane) nmb"
 /note="transmembrane glycoprotein"
 variation 195
 /allele="C"
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 variation 197
 /allele="H"
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 /db_xref="dbSNP:530413"
 Region 259..319

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/region_name="Repeats in polycystic kidney disease 1
(PKD1) and other proteins"
/note="PKD"
/db_xref="CDD:smart00089"
1..560
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/coded_by="NM_002510.1:92..1774"
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CDS

ORIGIN

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61  vwkrqdmrwk  nswkggrvqa  vltsdspalv  qsnitfavnl  ifprcqkeda  ngnivyeknc
121  rneaglsadp  yvynwtawse  dsdgenqtgq  shhnvfpdgk  pfphhpgwrr  wnfiyvfhtl
181  ggyfqklgrc  svrvsvntan  vtlgpqlmev  tvyrrhgray  vpiaqvkdvv  vvtddqipfv
241  tmfqkndrns  sdetflkdip  imfdvlihdv  shflnystin  ykwsfgdntg  lfvstnhtvn
301  htvylnqtfs  lnlvtkaaap  gpcppppppp  rpskptpslg  pagdnplels  ripdencqin
361  ryghfgatit  ivegilevni  iqmtdvlmpv  pwesslidf  vvtcqqsipt  evctiisdpt
421  ceitqntvcs  pvdvdemcll  tvrrtfngsq  tycvnltlqg  dtslaltstl  isvpdrdpas
481  plrmansali  svglclafvt  visllvykhh  keynpiensp  gnvvrskgls  vflnrakavf
541  fpgnqekdpl  lknqefkgvs
```

//

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Blast 2 Sequences results

PubMed

Entrez

BLAST

OMIM

Taxonomy

Structure

BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.5 [Nov-16-2002]

Matrix: BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.000 wordsize: 3 Filter ☐ Align ☐

Sequence 1 lc|seq_1 Length 121

NMB

NP_066563

Sequence 2 lc|seq_2 Length 560

6 PNMB

NP_002501

No significant similarity was found



results of BLAST

BLASTP 2.2.6 [Apr-09-2003]

Reference:

Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

RID: 1051035808-05395-3586

Query=

(121 letters)

Database: All non-redundant GenBank CDS

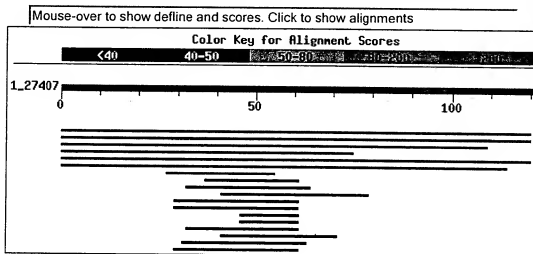
translations+PDB+SwissProt+PIR+PRF

1,415,660 sequences; 455,667,871 total letters

If you have any problems or questions with the results of this search please refer to the [BLAST FAQs](#)

[Taxonomy reports](#)

Distribution of 18 Blast Hits on the Query Sequence



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Sequences producing significant alignments:

	Score	E
	(bits)	Value
gi 10835107 ref NP_066563.1 neuromedin B [Homo sapiens] >g...	149	9e-36
gi 120141490 sp P08949 NEUB HUMAN Neuromedin B-32 precursor ...	131	2e-30
gi 13938517 gb AAH07407.1 AAH07407 Similar to neuromedin B ...	118	2e-26
gi 88253 pir A28945 neuromedin B precursor - human	103	4e-22

gi 13386018 ref NP_080799.1 	RIKEN cDNA 3110023K12 [Mus mus...	93	9e-19	L
gi 112182 pir A37178	neuromedin B precursor - rat	91	5e-18	
gi 128094 sp P01297 NEUB_PIG	Neuromedin B-32 [Contains: Neu...	52	1e-06	
gi 121641 sp P29007 GRP_BOMOR	Gastrin-releasing peptide pre...	35	0.18	
gi 1237140 gb AAC59785.1 	SAP bombesin preprohormone	34	0.36	
gi 9049482 gb AAF82387.1 AF11028.1	gastrin-releasing pepti...	34	0.52	
gi 422599 pir A47201	bombesinlike peptide - African clawed...	33	0.63	
gi 1171692 sp P43443 NEUB_XENLA	Neuromedin B precursor >gi ...	33	0.69	
gi 1237138 gb AAC59784.1 	Phe-13 bombesin preprohormone >gi ...	33	0.72	
gi 115097 sp P01296 BOMB_BOMVA	Bombesin precursor >gi 25763...	32	2.3	
gi 115096 sp P21591 BOMB_BOMOR	Bombesin precursor >gi 10397...	31	2.8	
gi 87496 pir A26182	gastrin-releasing peptide precursor sp...	30	5.0	
gi 1346185 sp P47851 GRP_SHEEP	Gastrin-releasing peptide pr...	30	7.8	
gi 2506229 sp P08947 LITP_PHYSA	[Phe8]-phyllolitorin precu...	30	8.6	

Alignments

Get selected sequences

Select all

Deselect all

└─>[gi|10835107|ref|NP_066563.1|](#) **L** neuromedin B [Homo sapiens]

[gi|189228|gb|AAA59934.1|](#) **L** neuromedin B

Length = 121

Score = 149 bits (376), Expect = 9e-36

Identities = 90/121 (74%), Positives = 90/121 (74%)

Query: 1 MARRAGGARMFGSXXXXXXXXXXXXXXXSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60

MARRAGGARMFGS SWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS

Sbjct: 1 MARRAGGARMFGSLLLLFALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60

Query: 61 LEPSSPSHWGQLPTPLRDQXXXXXXXXXXXXXXXXXGVLSRPAQIQYRRLLVQILQ 120

LEPSSPSHWGQLPTPLRDQ GVSLSRPAQIQYRRLLVQILQ

Sbjct: 61 LEPSSPSHWGQLPTPLRDQLQLSHDLLGILLKKALGVLSRPAQIQYRRLLVQILQ 120

Query: 121 K 121

K

Sbjct: 121 K 121

└─>[gi|20141490|sp|P08949|NEUB_HUMAN](#) Neuromedin B-32 precursor [Contains: Neuromedi

[gi|14250345|gb|AAH08603.1|AAH08603](#) **L** neuromedin B [Homo sapiens]

Length = 121

Score = 131 bits (329), Expect = 2e-30

Identities = 82/121 (67%), Positives = 82/121 (67%)

Query: 1 MARRAGGARMFGSXXXXXXXXXXXXXXXSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60

MARRAGGARMFGS SWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS

Sbjct: 1 MARRAGGARMFGSLLLLFALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60

Query: 61 LEPSSPSHWGQLPTPLRDQXXXXXXXXXXXXXXXXXGVLSRPAQIQYRRLLVQILQ 120

LEPSSPS G LRDQ GVSLSRPAQIQYRRLLVQILQ

Sbjct: 61 LEPSSPSPLGTATHTSLRDQLQLSHDLLGILLKKALGVLSRPAQIQYRRLLVQILQ 120

Query: 121 K 121
K
Sbjct: 121 K 121

⌈>gi|13938517|gb|AAH07407.1|AAH07407 Similar to neuromedin B [Homo sapiens]
gi|13938561|gb|AAH07431.1|AAH07431 Similar to neuromedin B [Homo sapiens]
Length = 154

Score = 118 bits (295), Expect = 2e-26
Identities = 71/110 (64%), Positives = 71/110 (64%)

Query: 1 MARRAGGARMFGSXXXXXXXXXXXXXSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60
MARRAGGARMFGS SWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS
Sbjct: 1 MARRAGGARMFGSLLLFALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60
Query: 61 LEPSSPSHWGQLPTPLRDQRXXXXXXXXXXXXXGVLSRPAPQIQ 110
LEPSSPS G LRDQR GVLSRPAPQIQ
Sbjct: 61 LEPSSPSPLGTATHTSLRDQRLQLSHDLLGILLKKALGVLSRPAPQIQ 110

⌈>gi|88253|pir||A28945 neuromedin B precursor - human
Length = 76

Score = 103 bits (258), Expect = 4e-22
Identities = 62/76 (81%), Positives = 62/76 (81%)

Query: 1 MARRAGGARMFGSXXXXXXXXXXXXXSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60
MARRAGGARMFGS SWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS
Sbjct: 1 MARRAGGARMFGSLLLFALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60
Query: 61 LEPSSPSHWGQLPTTP 76
LEPSSPSHWGQLPTTP
Sbjct: 61 LEPSSPSHWGQLPTTP 76

⌈>gi|13386018|ref|NP_080799.1| [L] RIKEN cDNA 3110023K12 [Mus musculus]
gi|20139148|sp|Q9CR53|NEUB_MOUSE Neuromedin B-32 precursor [Contains: Neuromedin
gi|12848356|dbj|BAB27922.1| [L] unnamed protein product [Mus musculus]
gi|12851724|dbj|BAB29144.1| [L] unnamed protein product [Mus musculus]
gi|20306611|gb|AAH28490.1| RIKEN cDNA 3110023K12 [Mus musculus]
Length = 121

Score = 92.8 bits (229), Expect = 9e-19
Identities = 61/121 (50%), Positives = 68/121 (56%)

Query: 1 MARRAGGARMFGSXXXXXXXXXXXXXSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60
M R+AG + + +WDLPEPRSRASKIRVH RGNLWATGHFMGKKS
Sbjct: 1 MTRQAGSSWLLRGLLLFALFASGVAPFNWDLPEPRSRASKIRVHPRGNLWATGHFMGKKS 60
Query: 61 LEPSSPSHWGQLPTPLRDQRXXXXXXXXXXXXXGVLSRPAPQIQIYRRLLVQILQ 120
LEP S S G P RDQR G++ S PAP IQYRRLL +LQ
Sbjct: 61 LEPPSLSLVGTAFFNTPRDQRLQLSHDLLRIILLRKKALGMNFGSGPAPPIQYRRLLLEPLLQ 120
Query: 121 K 121

K
Sbjct: 121 K 121

└─>gi|112182|pir||A37178 neuromedin B precursor - rat
Length = 117

Score = 90.5 bits (223), Expect = 5e-18
Identities = 59/115 (51%), Positives = 64/115 (55%)

Query: 1 MARRAGARMFGSXXXXXXXXXXXXXSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS 60
M R+AG + SWDLPEPRSRASKIRVH RGNLWATGHFMGKKS

Sbjct: 1 MTRQAGSTWLLRGLLLFALFVSGITPFSWDLPEPRSRASKIRVHPRGNLWATGHFMGKKS 60

Query: 61 LEPSSPSHWGQLPTPLRDQRXXXXXXXXXXXXXGVSLSRPAPQIQYRRL 115

LEP S S G P R+QR G++LS PAP IQYRRL

Sbjct: 61 LEPPSLSLVGTAPPITQREQLQLSHDLLRILLQKALGMNLSGPAPPIQYRRL 115

└─>gi|128094|sp|P01297|NEUB_PIG Neuromedin B-32 [Contains: Neuromedin B]
gi|69282|pir||BSPGNB neuromedin B-32 -.pig
Length = 32

Score = 52.4 bits (124), Expect = 1e-06
Identities = 27/29 (93%), Positives = 27/29 (93%)

Query: 28 SWDLPEPRSRASKIRVHSRGNLWATGHFM 56
SWDLPEPRSR KIRVH RGNLWATGHFM

Sbjct: 4 SWDLPEPRSRAGKIRVHPRGNLWATGHFM 32

└─>gi|121641|sp|P29007|GRP_BOMOR Gastrin-releasing peptide precursor (GRP-29) [Cor
Neuromedin C (GRP-10); C-terminal extension peptide
(CTEP)]

gi|283791|pir||A42437 gastrin-releasing peptide - Bombina orientalis

gi|211019|gb|AAA51409.1 gastrin-releasing peptide

Length = 155

Score = 35.4 bits (80), Expect = 0.18
Identities = 14/25 (56%), Positives = 19/25 (76%)

Query: 38 ASKIRVHSRGNLWATGHFMGKKSLE 62

AS +++ RG+ WA GH MGRKS+E

Sbjct: 42 ASLSKIYPRGSHWAVGHLMGKKSIE 66

└─>gi|1237140|gb|AAC59785.1 SAP bombesin preprohormone
Length = 119

Score = 34.3 bits (77), Expect = 0.36
Identities = 15/33 (45%), Positives = 21/33 (63%)

Query: 33 EPRSRASKIRVHSRGNLWATGHFMGKKSLEPSS 65

+P ++ S GN WA GHFMGKKS+ ++

Sbjct: 35 DPNNQGLSLQQLGNQWARGHFMGKKSLODTN 67

┌>gi|9049482|gb|AAF82387.1|AF111028.1 gastrin-releasing peptide precursor [Caras:
Length = 157

Score = 33.9 bits (76), Expect = 0.52
Identities = 19/43 (44%), Positives = 23/43 (53%), Gaps = 5/43 (11%)

Query: 42 RVHSRGNLWATGHFMGKKS----LEPSSPSHWGQLPTPLRDQ 80
+V+ RGN WA GH MGKKS + P P G + RDQ
Sbjct: 35 KVYPRGNHWAVGHLMGKKSTDEQVRPEDPED-GDETSMTTRDQ 76

┌>gi|422599|pir||A47201 bombesinlike peptide - African clawed frog
Length = 120

Score = 33.5 bits (75), Expect = 0.63
Identities = 18/33 (54%), Positives = 20/33 (60%), Gaps = 3/33 (9%)

Query: 30 DLPEPRSRASKIRVHSRGNLWATGHFMGKKSLE 62
+ E KIR RGN WA GHFMGKKS+
Sbjct: 31 EFSEDARNIEKIR---RGNQWAI GHFMGKKS LQ 60

┌>gi|1171692|sp|P43443|NEUB_XENLA Neuromedin B precursor
gi|214614|gb|AAA49912.1| neuromedin
Length = 120

Score = 33.5 bits (75), Expect = 0.69
Identities = 18/33 (54%), Positives = 20/33 (60%), Gaps = 3/33 (9%)

Query: 30 DLPEPRSRASKIRVHSRGNLWATGHFMGKKSLE 62
+ E KIR RGN WA GHFMGKKS+
Sbjct: 31 EFSEDARNIEKIR---RGNQWAI GHFMGKKS LQ 60

┌>gi|1237138|gb|AAC59784.1| Phe-13 bombesin preprohormone
gi|1589538|prf||2211320A bombesin
Length = 119

Score = 33.5 bits (75), Expect = 0.72
Identities = 13/16 (81%), Positives = 14/16 (87%)

Query: 47 GNLWATGHFMGKKSLE 62
GN WA GHFMGKKS+
Sbjct: 49 GNQWAVGHFMGKKS LQ 64

┌>gi|115097|sp|P01296|BOMB_BOMVA Bombesin precursor
gi|25763397|pir||BSTDY bombesin precursor - yellow-bellied toad
gi|65309|emb|CAA36686.1| bombesin [Bombina variegata]
Length = 107

Score = 31.6 bits (70), Expect = 2.3
Identities = 12/16 (75%), Positives = 13/16 (81%)

Query: 47 GNLWATGHFMGKKSL 62
GN WA GH MGKKSL+
Sbjct: 46 GNQWAVGHLMGKKSLQ 61

gi|115096|sp|P21591|BOMB_BOMOR Bombesin precursor
gi|103971|pir||A39261 bombesin precursor - Bombina orientalis
gi|211017|gb|AAA48551.1| bombesin
Length = 119

Score = 31.2 bits (69), Expect = 2.8
Identities = 15/31 (48%), Positives = 19/31 (61%), Gaps = 1/31 (3%)

Query: 33 EPRSRSKIRVHSR-GNLWATGHFMGKKSL 62
E + +I + R GN WA GH MGKKSL+
Sbjct: 34 EDPNNQGRISLQRLGNQWAVGHLMGKKSLQ 64

gi|87496|pir||A26182 gastrin-releasing peptide precursor splice form III - hum:
Length = 138

Score = 30.4 bits (67), Expect = 5.0
Identities = 18/32 (56%), Positives = 21/32 (65%), Gaps = 1/32 (3%)

Query: 42 RVHSRGNLWATGHFMGKKSL-EPSSPSHWQL 72
+++ RGN WA GH MGKKS E SS S G L
Sbjct: 36 KMYPRGNHWA VGHLMGKKSTGESSSVSERSGL 67

gi|1346185|sp|P47851|GRP_SHEEP Gastrin-releasing peptide precursor (GRP) [Cont:
(GRP-10)]
gi|2136897|pir||I47010 gastrin-releasing peptide - sheep
gi|913168|gb|AAB32675.1| Gastrin-releasing peptide GRP [Ovis aries]
Length = 134

Score = 30.0 bits (66), Expect = 7.8
Identities = 17/42 (40%), Positives = 24/42 (57%), Gaps = 9/42 (21%)

Query: 32 PEPRSRSASKI-----RVHSRGNLWATGHFMGKKSL 64
P PR A+ + +++++RGN WA GH MGKKS+ S
Sbjct: 17 PAPRGSAAPVTAGRAGALAKMYTRGNHWA VGHLMGKKSVAS 58

gi|2506229|sp|P08947|LITP_PHYSA [Phe8]-phyllolitorin precursor
gi|1362698|pir||B57058 Phe-8 phyllolitorin precursor - Sauvage's leaf frog
gi|998450|gb|AAB32788.1| Phe8 phyllolitorin [Phyllomedusa sauvagei]
Length = 90

Score = 29.6 bits (65), Expect = 8.6
Identities = 17/33 (51%), Positives = 19/33 (57%), Gaps = 1/33 (3%)

Query: 30 DLPEPRSRSKIRVHSRGNLWATGHFMGKKSL 62

++E SK V R LWA G FMGKKSLE
Sbjct: 32 EVTEESDDLKSRNVLQR-QLWAVGSFMGKKSLE 63

☐ Get selected sequences☐ Select all☐ Deselect all

Database: All non-redundant GenBank CDS
translations+PDB+SwissProt+PIR+PRF
Posted date: Apr 21, 2003 1:41 AM
Number of letters in database: 455,667,871
Number of sequences in database: 1,415,660

Lambda	K	H
0.319	0.134	0.424

Gapped Lambda	K	H
0.267	0.0410	0.140

Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Hits to DB: 89,060,364
Number of Sequences: 1415660
Number of extensions: 2728065
Number of successful extensions: 4328
Number of sequences better than 10.0: 24
Number of HSP's better than 10.0 without gapping: 23
Number of HSP's successfully gapped in prelim test: 1
Number of HSP's that attempted gapping in prelim test: 4305
Number of HSP's gapped (non-prelim): 24
length of query: 121
length of database: 455,667,871
effective HSP length: 97
effective length of query: 24
effective length of database: 318,348,851
effective search space: 7640372424
effective search space used: 7640372424
T: 11
A: 40
X1: 16 (7.4 bits)
X2: 38 (14.6 bits)
X3: 64 (24.7 bits)
S1: 41 (21.8 bits)
S2: 65 (29.6 bits)